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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF APPEALS AND INTERFERENCES

Application of:	Kohn, et al.
Serial No.:	08/225,478
Filed:	April 8, 1994
For:	Gene Therapy by Administration of Genetically Engineered $CD34^+$ Cells Obtained from Cord Blood
Group:	1632
Examiner:	Campell

Assistant Commissioner of Patents
Washington, DC 20231

BRIEF BEFORE THE BOARD OF APPEALS AND INTERFERENCES

Sir:

This is an Appeal from the Final Rejection dated August 20, 1998.

Real Parties in Interest

The real parties in interest are the Children's Hospital of Los Angeles, the Government of the United States of America as represented by Secretary, Department of Health and Human Services, and Genetic Therapy, Inc., the assignees of the claimed subject matter of the above-identified application.

Related Appeals and Interferences

There are no related appeals and interferences with respect to the above-identified application.

Status of Claims

Claims 16-20 have been cancelled.

Claims 6-15 and 23-26 have been allowed.

Claims 1-3, 5, 21, and 22 are pending, stand finally rejected, and are before the Board on Appeal. Claim 4 has been objected to. Claims 1-5, 21, and 22 are listed in the Appendix attached hereto.

Status of Amendments

The claims have not been amended after the Final Rejection.

Summary of the Invention

The present invention is directed to a method of expressing a therapeutic agent in a human. As defined broadly in Claim 1, the method comprises administering autologous CD34+ cells obtained from cord blood to the human. The autologous CD34+ cells have been genetically engineered to include at least one nucleic acid sequence encoding a therapeutic agent. Support is found in the specification in the second full paragraph of Page 3, and in Example 2. The nucleic acid sequence may be contained in a viral vector, as defined in Claim 2. The viral vector may be a retroviral vector, as defined in Claim 3. Support is found in the specification in the first three paragraphs of Page 4. The CD34+ cells may be administered in an amount of from about $5x10^5$/kg to about $10x10^7$/kg, as defined in Claim 5. Support is found in the specification at Page 9.

Issues Presented and Grouping of Claims

Claims 1-3, 5, 21, and 22 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited to methods of treating severe combined immunodeficiency syndrome using therapeutic gene transfer to autologous CD34+ cells obtained from cord blood cells, wherein said cells have been genetically engineered with a nucleic acid sequence encoding adenosine deaminase

(ADA), and further, wherein said cord blood cells are administered to a patient such that said ADA is expressed in an amount sufficient to provide a therapeutic effect, does not reasonably provide enablement for the treatment of any and all diseases with any and all cells and nucleic acids.

The Examiner has taken the position that Applicants have not tendered any evidence or argument to support that undue experimentation would not have been required to have expressed therapeutic agents in humans. The Examiner states that two references, cited during prosecution of the above-identified application, namely, the Kohn 1995 paper and the Orkin reference entitled, "Report and Recommendations of the Panel to Assess the NIH Investment in Research on Gene Therapy," show that undue experimentation is required to have expressed therapeutic agents in humans.

The Examiner also has taken the position that Applicants have not shown that the CD34+ cells, once transduced, would have been able to effect the therapeutic expression of an agent in a human.

The rejected claims stand or fall together.

Argument

The burden is upon the Examiner to show that one cannot genetically engineer autologous CD34+ cells with a nucleic acid sequence encoding a therapeutic agent, and/or cannot administer such genetically engineered cells to the human for expression of the therapeutic agent in the human. (See In Re Marzocchi, 169 U.S.P.Q. 367 (C.C.P.A. 1971).)

As the Examiner admits, Applicants have demonstrated the genetic engineering of autologous CD34+ cells obtained from cord blood, and the administration of such cells to

an infant, whereby such cells express adenosine deaminase in the infant. Thus, Applicants have demonstrated the principle that one may genetically engineer autologous CD34+ cells obtained from cord blood with a nucleic acid sequence encoding a therapeutic agent, and administer the cells to a human, whereby the therapeutic agent is expressed in the human.

Applicants need not demonstrate that autologous CD34+ cells obtained from cord blood can be engineered with every possible nucleic acid sequence encoding a therapeutic agent and that each therapeutic agent be expressed in the human once the genetically engineered cells are administered to the human. (See Ex parte Mark, 12 U.S.P.Q.2d 1904 (Bd. App. Int. 1989).) Because Applicants have demonstrated that adenosine deaminase can be expressed in a human by practicing the claimed method, one skilled in the art would expect reasonably that autologous CD34+ cells obtained from cord blood could be genetically engineered with nucleic acid sequences encoding other therapeutic agents, and that such cells may be administered to a human, whereby such therapeutic agents may be expressed in the human.

The "evidence" of nonenablement provided by the Examiner merely states that further work needs to be done with respect to engineering CD34+ cells with genes other than ADA (Kohn, 1995), and that problems remain in various aspects of gene therapy (Orkin). These references, however, do not state that the various problems associated with gene therapy cannot be overcome, or that CD34+ cells cannot be genetically engineered with genes other than the ADA gene. In fact, the Orkin paper states that "More than 100 clinical protocols for gene therapy have been reviewed and approved by the RAC and subsequently approved by the NIH Director. (Table 3). Indeed, 597

individuals have already undergone gene transfer in experiments involving more than a dozen diseases." Thus, even the Orkin report cited by the Examiner provides a reasonable expectation to one of ordinary skill in the art that gene transfer will be successful for expressing a variety of therapeutic agents.

Thus, the Examiner has provided no evidence, other than speculative statements, which would indicate to one skilled in the art that proteins other than ADA could not be expressed in accordance with the claimed method. Therefore, the Examiner cannot assert that the claimed method is not enabling for nucleic acid sequences other than the ADA gene, and, therefore, the Examiner has not met his burden in showing that the specification is not enabling with respect to genes other than the ADA gene.

For the above reasons and others, the specification provides an enabling disclosure within the meaning of 35 U.S.C. 112, first paragraph, and it is therefore respectfully requested that the rejection under 35 U.S.C. 112, first paragraph be reversed.

Respectfully submitted,

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Signature
7/2/99
Date of Signature

APPENDIX - CLAIMS ON APPEAL

1. A method of expressing a therapeutic agent in a human, comprising:

administering autologous CD34+ cells obtained from cord blood to said human, said autologous CD34+ cells having been genetically engineered to include at least one nucleic acid sequence encoding a therapeutic agent.

2. The method of Claim 1 wherein said at least one nucleic acid sequence is contained in a viral vector.

3. The method of Claim 2 wherein said viral vector is a retroviral vector.

4. The method of Claim 1 wherein said therapeutic agent is adenosine deaminase.

5. The method of Claim 1 wherein said CD34+ cells are administered in an amount of from about $5x10^5$/kg to about $10x10^7$/kg.

21. The method of Claim 5 wherein said CD34+ cells are administered in an amount of from about $5x10^5$/kg to about $1x10^7$/kg.

22. The method of Claim 21 wherein said CD34+ cells are administered in an amount of from about $5x10^5$/kg to about $5x10^6$/kg.